HEPATITIS C VIRUS INFECTION AMONG THAI BLOOD DONORS : ANTIBODY PREVALENCE, RISK FACTORS AND DEVELOPMENT OF RISK SCREENING FORM

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Abstract. Hepatitis C virus (HCV) infection is an important blood-borne infection in many countries, including Thailand. For epidemiological surveillance and controlling the infection, 2,167 blood donors were screened for antibody to HCV by an enzyme immunoassay method and interviewed by using a structured questionnaire which consisted of personal health history and some risk behaviors. The prevalence and risk factors were assessed and the risk screening form was developed. The results revealed that the prevalence of anti-HCV was 2.90%. Male blood donors had relatively higher anti-HCV positive rate than females (3.21% *vs* 1.77%). The significant risk factors from univariate analysis were: (a) gender as male, OR=1.94 (p=0.042), (b) education to the primary level, OR=4.15 (p<0.001), (c) occupation as laborer or agriculture workers, OR=2.87 (p<0.001), police and military, OR=1.82 (p=0.046), (d) residence in a rural area, OR=3.09 (p<0.001), (e) a history of receiving blood or blood products, OR=5.21 (p<0.001), (f) a history of tattooing, OR=1.70 (p=0.043), (g) a history of IDU (Infecting Drug Use), OR=41.43 (p<0.001), (h) a history of STDs (sexually transmitted diseases) in the last year, OR=3.87 (p=0.021), and (i) a history of sexual service, OR=4.24 (p=0.017). After multivariate analysis, four variables related to HCV infection among the studied samples included education to the primary level, OR=3.34 (p=0.0036), occupation as a laborer or agriculture worker, OR=2.14 (p=0.0092), a history of receiving blood or blood products, OR = 4.13 (p=0.0029), and a history of IDU, OR=3.82 (p<0.0001).The risk screening form was developed using risk scores. The validity was calculated by the Receiving Operating Curve. The sensitivity of this form was approximately 55.3% and the specificity was 85.7% when a cut-off score at risk ≥7 was used. If the cut-off score was ≥6, the screening form showed 77.1% of specificity and 61.3% sensitivity. This risk screening form should be applied not only for blood donation but also for pre-marital health screening.

INTRODUCTION

Hepatitis C virus (HCV) infection is an important public health problem in many countries, including Thailand (Cohen ,1999; Holland *et al*, 2000; Nur *et al*, 2000; Luksamijarulkul *et al*, 2000; Daw *et al*, 2002). The virus had infected approximately 170 million people world-wide by the year 2000 and the trend of infection has increased in recent years (Cohen, 1999; Holland *et al*, 2000; Rosenberg *et al*, 2001). A wide range of clinical manifestrations occurs from asymptomatic chronic carriage to acute hepatitis (Zoulim *et al*, 2003). The complications from HCV are quite serious, 10-40% develop chronic hepatitis and gradual progression to liver cirrhosis and hepatocellular carcinoma (Tanikawa, 1994; Zoulim *et al*, 2003). Major transmission is via the parenteral route and a minority is via sexual contact (Stary *et al*, 1992; Luksamijarulkul *et al*, 2000; Romanowski *et al*, 2003). Sexual transmission of HCV may be increased among HIV-infected persons (Stary *et al*, 1992). In Thailand, the highest risk group of HCV infection was in the injecting drug user (IDU) group with 83-95% infection rates (Louisirirotchanakul *et al*, 1992; Luksamijarulkul and Plucktaweesak, 1996). The other risk

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group was in the female sex worker (FSW) group with 9.5% of infection (Luksamijarulkul and Daengbubpha, 1997). The sexual partners of IDUs and the clients of FSWs have an increased chance of acquiring HCV infection if they do not use condoms. Both of these infected groups can transmit the infection to the general population who may then donate blood. Previous studies reported that anti-HCV prevalence range from 0.2-1% in Europe and North America to 0.3-3.1% in Asia (Boonmar *et al*, 1995; Cohen, 1999; Nur *et al*, 2000; Holland *et al*, 2000; Daw *et al*, 2002). Recently, a study in blood donors in Northeastern Thailand showed a higher prevalence of HCV infection than donors in other parts of Thailand (Songsivilai *et al*, 1997). Some community hospitals in rural areas of Thailand lack the HCV antibody screening test for blood donation. Sexually active individuals are not screened for HCV before marriage. This study attempted to investigate the HCV antibody prevalence, risk factors among Thai blood donors and to develop a risk screening form for HCV infection. It is valuable for epidemiological surveillance. In addition, the risk screening form may be useful for application in rural community hospitals which lack the budget for HCV screening and for risk screening in pre-marital couples.

MATERIALS AND METHODS

Study design, study population and laboratory methods

The study design was a cross-sectional analytic study of 2,167 blood donors who attended the Regional Blood Center, Phitsanulok Province, Thailand. This regional blood center had the responsibility of receiving donated blood and blood products, then distributing these to other provinces in the Central and Northern regions of Thailand. All blood donors from July 1999 to June 2000 were included in the study. Although, anti-HCV antibody testing is routine practice for blood donation, only donors who voluntarily participated were interviewed, by using structured questionnaires, including socio-demographic variables and some risk behaviors. Before interview and blood donation, donors had received information regarding HCV infection. After that, donors were required to fill in the informed consent forms. The blood specimens which were collected from the studied blood donors were screened for anti-HCV antibody by an enzyme immunoassay, ABBOTT HCV EIA 3.0 (the third generation) with 99-100% sensitivity and 99.6% specificity. The cut-off values for anti-HCV positivity followed the criteria of the diagnostic kit. A specimen was considered positive if the antibody was positive on a repeat test.

Data analysis

From the laboratory results, the studied blood donors were divided into 2 groups; the first group was positive for anti-HCV antibody and the second group was negative for anti-HCV antibody. The information from interviews of the 2 groups was analyzed to search for risk factors for HCV infection among the studied blood donors, using an odds ratio (OR), 95% confidence interval of the OR, a chi-square test and multiple logistic regression analysis. A p-value less than 0.05 was considered to indicate statistical significance.

RESULTS

General characteristics of studied blood donors

Of the 2,167 studied blood donors, 49.25% were 16-30 years of age, 39.86% were 31-45 and 10.89% were 45-60. The mean age was 32 ±10 years. About 79% were male. Almost 54% of studied blood donors were married. Approximately 41% finished vocational or undergraduate school and nearly 23% finished primary education. One-third of the studied blood donors were police or military and another third were laborers or agriculture workers. Almost 60% came from urban areas. Half of them had a monthly income of more than 10,000 baht.

HCV antibody prevalence

Sixty-three donors (2.9%) were positive for anti-HCV antibody. The age group of 31-45 years showed the highest prevalence of anti-HCV (3.36%). Male blood donors had a relatively higher positive rate than females (3.21% *vs* 1.77%). Blood donors who finished only primary education had a relatively higher anti-HCV positive rate than donors who finished secondary education or higher. When the prevalence was classified by occupation, it was found that laborers or agriculture workers

Table 1
Prevalence of anti-HCV antibody among studied blood donors classified by some socio-demographic variables.

Socio-demographic variables	No. tested	Anti-HCV positive	
		No.	%
Age group (years)			
≤ 30	1,068	32	2.99
31-45	863	29	3.36
> 45	236	2	0.85
Gender			
Male	1,716	55	3.21
Female	451	8	1.77
Marital status			
Single	992	31	3.12
Married and divorced	1,175	32	2.72
Education			
Primary level	491	35	7.05
Secondary level	775	14	1.80
Vocational and undergraduate	896	14	1.56
Occupation			
Laborer or agriculture workers	686	30	4.37
Police and military	731	21	2.87
Governmental officer and state enterprise	322	5	1.55
Others (students and housewives)	442	7	1.58
Present residence			
Rural area	880	42	4.77
Urban area	1,287	21	1.63
Total	2,167	63	2.90

(4.37%) and police and military (2.87%) had relatively higher anti-HCV positive rates than the other groups. Details are shown in Table 1.

Risk factors for HCV infection

After univariate analysis, it was found that the significant risk factors for HCV infection among studied blood donors were: (a) gender as male, OR=1.94 (p=0.042), (b) education only to primary level, OR=4.15 (p<0.001), (c) occupation as a laborer or agriculture worker, OR=2.87 (p<0.001), police or military, OR=1.82 (p=0.046), (d) residence in a rural area, OR=3.09 (p<0.001), (e) a history of receiving blood or blood products, OR=5.21 (p<0.001), (f) a history of tattooing, OR=1.70 (p=0.043), (g) a history of IDU, OR=41.43 (p<0.001), (h) a history of STDs in the last year, OR=3.87 (p=0.021), and (i) a history of sexual service, OR=4.24 (p=0.017). Details are shown in Table 2.

Multiple logistic regression analysis was applied for controlling confounders and for evaluating the effects of risk variables on HCV infection in the studied group. The order variables were entered into the logistic regression model as follows: gender (p=0.042), education (p<0.001), occupation (p<0.001), present residence (p<0.001), a history of receiving blood or blood product (p<0.001), a history of tattooing (p=0.043), a history of IDU (p<0.001), a history of STDs (p=0.021), and a history of sexual service (p=0.017). After analysis, 4 variables related to HCV infection among studied samples included education to a primary level, OR=3.34 (p=0.0036), occupation as a laborer or agriculture worker, OR=2.14 (p=0.0092), a history of receiving blood or blood products, OR=4.13 (p=0.0029), and a history of IDU, OR=3.82 (p<0.0001), as shown in Table 3.

Table 2
Risk factors for HCV infection (positive HCV antibody) among studied blood donors by univariate analysis.

Risk factors	Crude odds ratio (OR)	95%CI of OR	p-value from χ^2 test
Socio-demographic factors			
Age			
≤ 30 years	0.89	0.53 , 1.48	0.711
> 30 years	1.00		
Gender			
Male	1.94	1.01 , 4.08	0.042[a]
Female	1.00		
Marital status			
Single	1.23	0.74 , 2.05	0.449
Married, divorced	1.00		
Education			
Primary level	4.15	2.59 , 6.65	< 0.001[a]
Secondary level and higher	1.00		
Occupation			
Laborer or agriculture workers	2.87	1.81 , 5.13	< 0.001[a]
Police and military	1.82	1.01 , 4.02	0.046[a]
Others	1.00		
Present residence			
Rural area	3.09	1.84 , 5.18	< 0.001[a]
Urban area	1.00		
History of risk behaviors			
History of receiving blood/blood products			
Yes	5.21	2.26 , 12.01	< 0.001[a]
No	1.00		
History of blood or secretion contact			
Yes	1.03	0.41 , 2.61	0.586
No	1.00		
History of tattooing			
Yes	1.70	1.02 , 2.86	0.043[a]
No	1.00		
History of injecting drug use			
Yes	41.43	17.52, 97.99	< 0.001[a]
No	1.00		
History of jaundice			
Yes	1.20	0.29 , 4.07	0.470
No	1.00		
History of STDs in the last year			
Yes	3.87	1.49 , 10.04	0.021[a]
No	1.00		
History of extramarital sex			
Yes	0.71	0.41 , 1.23	0.247
No	1.00		
History of sex service			
Yes	4.24	1.24, 13.10	0.017[a]
No	1.00		

[a]Statistical significance at $\alpha = 0.05$.

Table 3
Risk factors for HCV infection (positive HCV antibody) among studied blood donors by multivariate analysis (logistic regression analysis).

Risk factors	Adjusted OR	95% CI of OR	p-value
Education			
Primary level	3.34	1.80 , 10.15	0.0036
Secondary level and higher	1.00		
Occupation			
Laborer or agriculture worker	2.14	1.19 , 3.85	0.0092
Others	1.00		
History of receiving blood/blood products			
Yes	4.13	1.87 , 9.16	0.0029
No	1.00		
History of injecting drug use			
Yes	3.82	2.41 , 5.82	< 0.0001
No	1.00		

Development of a risk screening form for HCV infection, and its validity

The risk screening form for HCV infection among blood donors was developed by using risk scores from Table 3 as follows: risk score = scores of education + occupation + a history of receiving blood or blood products + a history of IDU. Score of education = 3 for primary level and lower, and = 0 for others. Score of occupation = 2 for a laborer or agriculture worker, and = 0 for others. Score of a history of receiving blood or blood products = 4 for having a history of receiving blood or blood products and 0 for having no history of receiving blood or blood products. Score of a history of IDU = 4 for having a history of IDU, and = 0 for having no history of IDU. The calculation of risk scores was analyzed and the validity of this model for predicting the risk for HCV infection among the studied donors was calculated by the Receiving Operating Curve (ROC). The sensitivity of this model was approximately 55.3% and the specificity was 85.7% when a cut-off score at risk ≥ 7 was used. If the cut-off score was ≥ 6, the screening form showed 77.1% of specificity and 61.3% sensitivity (Fig 1). A risk screening form for HCV infection among blood donors is proposed in Fig 2.

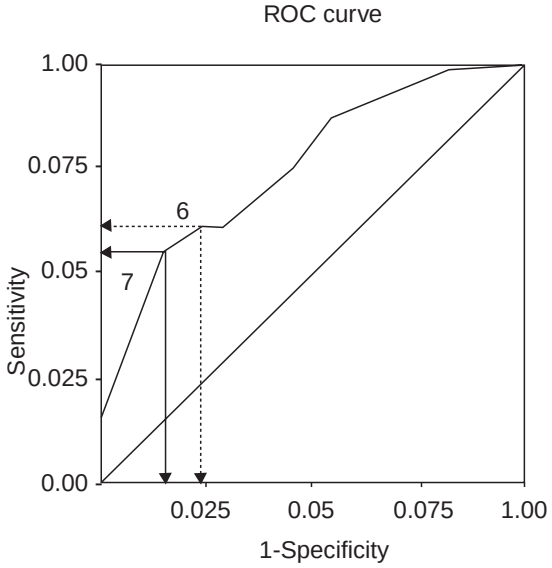

Fig 1–ROC curve for prediction of HCV infection among studied blood donors. When the cut-off score was ≥7, the screening form showed 85.7% specificity and 55.3% sensitivity analyzed by the ROC curve. If the cut-off score was ≥6, the screening form showed 77.1% specificity and 61.3% sensitivity.

DISCUSSION

The prevalence of a positive anti-HCV screen among the studied blood donors was 2.90% which was compared with previous studies in some groups of Thai blood donors, ranging from 1.5 to 4.5% (Boonmar *et al*, 1995; Songsivilai *et*

Risk screening form for HCV infection

Name ..... Age ..... years ..... months

Gender ☐ Male ☐ Female Marital status .....

Present residence…….

……Telephone…….

Risk factors			Full scores	Checklist scores
Education	:	Primary level	3	
		Secondary level and higher	0	
Occupation	:	Laborer or agriculture worker	2	
		Others	0	
History of receiving blood or blood products	:	Yes	4	
		No	0	
History of injecting drug use	:	Yes	4	
		No	0	
Total scores			13	

Interpretation : Total checklist scores ≥ 6 means you may be at risk for HCV infection with 61.3% sensitivity and 77.1 % specificity. You should check your blood sample due to the high risk for anti-HCV positive.

Fig 2–Risk screening form for HCV infection developed by using four predictors (education, occupation, history of receiving blood or blood products and a history of injecting drug use).

al, 1997). This study found that the prevalence in the age group 31- 45 years was relatively higher than in other age groups, but was not a statistically significant ($p>0.05$). Male blood donors had relatively higher prevalence than female blood donors. It was a significant risk factor (OR=1.94, $p=0.042$). This might be due to risk behaviors of males, *ie* outside socialization, extramarital sex and alcohol consumption as a risk factor for seeking female sex workers without condom use (Stary *et al*, 1992; Gilson *et al*, 1998). Donors with a marital status of being single had a higher anti-HCV prevalence than married blood donors, but this was not statistically significant ($p>0.05$). The study showed that anti-HCV positivity in the studied donors who finished only primary school was higher than in studied donors who finished secondary school and higher education. It was a significant risk factor (OR = 4.15, $p<0.001$). This supported the findings from previous studies that persons with low education had higher risk behaviors, such as, tattooing, injecting drug use and extramarital sex relations without condom use (Luksamijarulkul *et al*, 1998; Gilson *et al*, 1998).

Studied blood donors with occupations as laborers or agriculture workers had higher anti-HCV positivity than other occupations. This was a significant risk factor (OR=2.87, p<0.001 from univariate analysis and OR=2.14, p=0.0092 from multivariate analysis). Moreover, residence in a rural area was a significant risk factor for HCV infection among this group (OR=3.09, p<0.001). This indicates that a higher anti-HCV prevalence can be correlated with low socio-economic conditions, supported by several studies (Songsivilai *et al*, 1997; Luksamijarulkul *et al*, 2000; 2001). In addition, most blood donors living in rural areas finished only primary school and had occupations as laborers or agriculture workers.

Donors with a history of receiving blood or blood products had significant risk for positive anti-HCV (OR = 5.21, p<0.001) supported by other studies (Donahue *et al*, 1991; Daw *et al*, 2002). It was suggested that the possibility of infection might be due to the lack of the HCV screening or the low sensitivity of HCV screening test in a previous donation. A tattoo, which is an important risk factor for blood-borne infections like HBV infection was a significant risk factor for HCV infection among studied blood donors (OR= 1.73, p=0.043). However, it was not significant with multivariate analysis. Another risk factor was a history of injecting drug use (OR = 41.43, p<0.001) which is an important risk factor for HCV infection. Several reports showed a high prevalence of HCV infection in injecting drug users (Donahue *et al*, 1991; Luksamijarulkul and Plucktaweesak, 1996; Nur *et al*, 2000). There is no doubt that sexual activity is an important risk factor for the transmission of HIV and HBV but it seems to be of minor importance in the spread of HCV. This study found that a history of STDs in the last year and a history of sex service were significant risk factors for HCV infection with univariate analysis (OR=3.87, p=0.021 and OR=4.24, p=0.017, respectively) but they were not significant with multivariate analysis.

After multivariate analysis, the significant risk factors for positive anti-HCV or HCV infection were found in two socio-demographic variables, education to the primary level (OR= 3.34, p=0.0036) and occupation as laborer or agriculture worker (OR=2.14, p=0.0092) and two behavioral variables, a history of receiving blood or blood products (OR=4.13, p=0.0029) and a history of injecting drug use (OR=3.82, p<0.0001). The HCV risk screening form was developed by using predictors including these four variables. When the cut-off score was ≥ 7, the screening form showed 85.7% specificity and 55.3% sensitivity as analyzed by the ROC curve. If the cut-off score was ≥ 6, the screening form showed 77.1% specificity and 61.3% sensitivity. The blood donor who had a score ≥ 6 was considered as a potential risk for HCV infection, so he should not donate blood. The risk screening form for HCV infection in this study could be applied to pre-marital health screening or a pre-marital counseling clinic where the patient does not want blood screening. If he has a score ≥ 6, it can be recommended to have the screening due to a high risk for HCV infection.

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